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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER		see Form PCT/ISA/220	
P036716WO	ACTION	as well	as, where applicable, item 5 below.	
International application No.	International filing date (day/moni	h/year)	(Earliest) Priority Date (day/month/year)	
PCT/GB2005/000372	04/02/2005		06/02/2004	
Applicant				
MEDICAL RESEARCH COUNCIL				
This International Search Report has beer according to Article 18. A copy is being tra	n prepared by this International Sea Insmitted to the International Burea	rching Auth J.	nority and is transmitted to the applicant	
This International Search Report consists	of a total ofsh	eets.		
lt is also accompanied by	a copy of each prior art document of	ited in this	report.	
Basis of the report a. With regard to the language, the language in which it was filed, unl	international search was carried ou ess otherwise indicated under this i	on the bas	sis of the international application in the	
The international this Authority (Ru		of a transla	ation of the international application furnished to	
b. X With regard to any nucleo	otide and/or amino acid sequence	disclosed	in the international application, see Box No. I.	
2. Certain claims were fou	nd unsearchable (See Box II).			
3. X Unity of invention is lac	Unity of invention is lacking (see Box III).			
4. With regard to the title,				
X the text is approved as su				
the text has been establis	hed by this Authority to read as foll	ows:		
5. With regard to the abstract,				
X the text is approved as su	bmitted by the applicant.			
the text has been establis may, within one month from	shed, according to Rule 38.2(b), by om the date of mailing of this internation.	his Authori tional sear	ty as it appears in Box No. IV. The applicant ch report, submit comments to this Authority.	
6. With regard to the drawings ,				
a. the figure of the drawings to be p	published with the abstract is Figure	No. <u>3A</u>		
X as suggested by				
	is Authority, because the applicant	•		
	is Authority, because this figure bet e published with the abstract.	er criaracte	enzes the Hivehtion.	
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International application No.

:	INTERNATIONAL SEARCH REPORT	PCT/GB2005/000372	
Вох	ox No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)		
1.	. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:		
	a. type of material X a sequence listing table(s) related to the sequence listing		
	b. format of material X in written format X in computer readable form		
	c. time of filing/furnishing X contained in the international application as filed filed together with the international application in computer readable form X furnished subsequently to this Authority for the purpose of search		
2.	In addition, in the case that more than one version or copy of a sequence listing or furnished, the required statements that the information in the subsequent or a application as filed or does not go beyond the application as filed, as appropriate	dditional copies is identical to that in the	
3.	Additional comments:		

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PCT/GB2005/000372

A. CLASSII	C12N15/81 C12N15/63 C12N15/7	75 C12P21/02			
	According to International Patent Classification (IPC) or to both national classification and IPC				
	SEARCHED currentation searched (classification system followed by classification)	on symbols)			
C12N		on symbols,			
Documentat	ion searched other than minimum documentation to the extent that s	such documents are included in the fields se	earched		
Electronic d	ata base consulted during the international search (name of data ba	se and, where practical, search terms used)		
EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE, EMBASE, CHEM ABS Data					
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where appropriate, of the rel	evant passages	Relevant to claim No.		
х	KITAZONO ANA A ET AL: "Marker-fu for one-step mutagenesis of esser genes in yeast" YEAST,		1-9, 18-40		
	VeASI, vol. 19, no. 2, 30 January 2002 (2002-01-30), pages 141-149, XP002353151 ISSN: 0749-503X *Whole document, in particular: Abstract				
	and figures 1 and 3*				
ı					
		•			
X Furti	ner documents are listed in the continuation of box C.	Patent family members are listed in	n annex.		
i '	Special categories of cited documents:				
consid	"A" document defining the general state of the art which is not considered to be of particular relevance considered to				
filing d	filing date "L" document which may throw doubts on priority claim(s) or "L" document which may throw doubts on priority claim(s) or "A document of particular reference, are claimed with the document to cannot be considered to involve an inventive step when the document is taken alone				
citatio	which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or cited to establish the publication date of another cannot be considered to involve an inventive step when the document is combined with one or more other such document is combined.				
	ent published prior to the international filing date but	ments, such combination being obvior in the art. "&" document member of the same patent			
<u> </u>	nan the priority date claimed actual completion of the international search	Date of mailing of the international sea			
18 November 2005		2006_			
Name and r	nailing address of the ISA	Authorized officer			
	European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl,	DIN CAO DE MEI O DA	DDF		
	Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 BULCAO DE MELO BARRE				

International Application No
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C.(Continua	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MURPHY C K ET AL: "A double counter-selection system for the study of null alleles of essential genes in Escherichia coli" GENE, ELSEVIER, AMSTERDAM, NL, vol. 155, no. 1, 1995, pages 1-7, XP004042435 ISSN: 0378-1119 *Whole document, in particular: Abstract and figure 1*	1-9, 18-40
Α	LUCA F C ET AL: "MOB1, an essential yeast gene required for completion of mitosis and maintenance of ploidy" MOLECULAR BIOLOGY OF THE CELL, BETHESDA, MD, US, vol. 9, no. 1, January 1998 (1998-01), pages 29-46, XP002338945 ISSN: 1059-1524 cited in the application *Whole document, in particular: Abstract and Material and Methods*	1-9, 18-40
A _.	GEYMONAT MARCO ET AL: "In vitro regulation of budding yeast Bfal/Bub2 GAP activity by Cdc5." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 17, 25 April 2003 (2003-04-25), pages 14591-14594, XP002353152 ISSN: 0021-9258 *Whole document, in particular: Abstract and Material and Methods*	1-9, 18-40
Α	CROSS FREDERICK R: "'Marker Swap' plasmids: Convenient tools for budding yeast molecular genetics" YEAST, vol. 13, no. 7, 1997, pages 647-653, XP002353153 ISSN: 0749-503X *Whole document, in particular: Abstract and Material and Methods*	1-9, 18-40
A	ZHANG REN ET AL: "DEG: A Database of Essential Genes." NUCLEIC ACIDS RESEARCH, vol. 32, no. Database Issue, 1 January 2004 (2004-01-01), pages D271-D272, XP002353154 ISSN: 0305-1048 cited in the application *Whole document*	1-9, 18-40

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT Category * Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.	
outego.y			
A	SIKORSKI R S ET AL: "20 IN-VITRO MUTAGENESIS AND PLASMID SHUFFLING: FROM CLONED GENE TOMUTANT YEAST" METHODS IN ENZYMOLOGY, ACADEMIC PRESS INC, SAN DIEGO, CA, US, vol. 194, 1991, pages 302-318, XP002912110 ISSN: 0076-6879 cited in the application *Whole document, in particular: figure 1*	1-9, 18-40	
Α ,	*Whole document, in particular: figure 1* ELLEDGE S J ET AL: "A FAMILY OF VERSATILE CENTROMERIC VECTORS DESIGNED FOR USE IN THE SECTORING-SHUFFLE MUTAGENESIS ASSAY IN SACCHAROMYCES CEREVISIAE" GENE, ELSEVIER, AMSTERDAM, NL, vol. 70, no. 2, 30 October 1988 (1988-10-30), pages 303-312, XP000000376 ISSN: 0378-1119 cited in the application *Whole document, in particular: Abstract and figure 1*	1-9, 18-40	
	.*.		

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International application No. _PCT/GB2005/000372

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: .
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. X No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-9 (completely) and 18-40 (partially)
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-9 (completely) and 18-40 (partially)

Invention 1 concerns a cell that express both chromosomal genes and extra-chromosomal genes, wherein (a) the expressed extra-chromosomal genes include a gene with an essential function, the expression of which is unconditionally required for survival of the cell, (b) the chromosomal genes do not provide that essential function, and (c) the extra-chromosomal genes include a heterologous gene, the expression of which is controlled by a promoter that is functional in the cell. Invention 1 further concerns a method for preparing said cell, as well as the starting and intermediate cells used in said method.

2. claims: 10-14 (completely) and 18-40 (partially)

Invention 2 concerns a vector comprising (a) an essential gene whose expression is unconditionally required for survival of a cell of interest, (b) a conditionally-required gene to allow selection of host cells which include the vector, and (c) a gene encoding a heterologous protein of interest operably linked to a promoter that is functional in the cell of interest. Invention 2 further concerns a method for preparing a cell by transforming it with said vector.

3. claims: 15-17 (completely) and 18-40 (partially)

Invention 3 concerns a vector comprising (a) an essential gene whose expression is unconditionally required for survival of a cell of interest, (b) a conditionally-lethal gene to allow selective killing of host cells which include the vector, wherein the essential gene is MOB1, Cdc33 or Hsp10. Invention 3 further concerns a method for preparing a cell by transforming it with said vector.